typographical error. New claims 29-39 are supported throughout the specification, specifically on page 2, lines 19-24, and on page 10, lines 9-19.

No new matter is added. Reconsideration of the subject application is respectfully requested.

Sequence compliance

Applicants thank the Examiner for accepting the CRF and paper copy of the sequence listing. The specification is amended herein to refer to the appropriate sequence identifiers on page 13. Applicants submit that the application now satisfies the requirements of 37 C.F.R. § 1.821 (d).

Priority Documents

Applicants thank the Examiner for acknowledging receipt of the foreign priority document. Applicants note that products of binding M3 protein or a homolog thereof to a solid substrate (a "coupled protein") can be found in GB9916703. For example, a coupled protein is described at page 2, lines 33-34.

Formal Drawings

Applicants request that the requirement for new formal drawings be deferred until allowance of the subject application.

Description of the Drawings

As requested in the Office action, the specification is amended herein to cancel the description of the drawings previously found in the specification as filed on pages 7-8. Applicants note that the specification was amended previously to include this information in a section entitled "Brief Description of the Drawings."

Informalities

Claim 20 is amended to correct the typographical error in "fractalkine."

Dependent Form

The Office action alleges that claims 24-26 and 28, drawn to a labeled or a coupled M3 protein or chemokine, are broader than claim 17, and therefore alleges that claims 24-26 and 28 improperly depend from claim 17. Applicants respectfully disagree with this assertion.

The term "M3 protein" or "chemokine" includes both unlabeled and labeled forms of these molecules. As such, the genus of "M3 proteins" includes both labeled and unlabeled forms of the proteins; a "labeled M3 protein" is a subset of the genus of "M3 proteins." Similarly, the genus of "chemokines" includes both labeled and unlabeled forms of the chemokines; and a "labeled chemokine" is a subset of the genus of "chemokines." As such, Applicants submit that claims 24-26 and 28 properly depend from claim 17. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejections Under 35 U.S.C. §112, second paragraph

Claims 17-20 and 22-28 were rejected as allegedly being indefinite in the recitation of "M3." Applicants have amended the claims to refer to "M3 protein of MHV68," as requested in the Office action, thereby removing the rejection.

Rejections Under 35 U.S.C. §112, first paragraph

Claims 17-20 and 22-28 were rejected as allegedly the specification does not provide enablement for one of skill in the art to make and use a functional homolog of the M3 protein of MHV68. Applicants respectfully disagree with this assertion.

Applicants submit that homologs of the M3 protein of MHV68 can readily be identified by one of skill in the art using the guidance provided by the specification. For example, fusion proteins, derivatives, and fragments of M3 are described in the specification on page 6, line 28, to page 7, line 4. Guidance is also provided in the specification on page 18, line 29 to page 19, line 14. It should also be noted that van Berkel et al. (*J. Virol.* 74:6741-6747, 2000, previously cited) discuss MHV68 homologs (see page 6746, last paragraph of the discussion).

Furthermore, claim 17 has been amended to recite that the homolog binds the chemokine of interest. This amendment was discussed with Examiner Spiegler in the telephone conference of August 8, 2001. As discussed with Examiner Spiegler, binding assays using a labeled chemokine are described in the specification on page 9, line 1-10. One of skill in the art could readily use the assays described in the specification to determine if a homolog of M3 binds a chemokine of interest. Thus,

one of skill in the art can readily identify M3 homologs (such as a homolog isolated from another gammaherpesvirus) that can be used in the methods of the present invention.

Thus, Applicants submit that claims 17-20 and 22-28 are fully enabled by the specification. Reconsideration and withdrawal of the rejection are respectfully requested.

Claims 17-20 and 22-28 are rejected as the specification is allegedly not enabling to make and use the claimed methods with "any" chemokine. However, the Office action acknowledges that the specification is enabling for a method of blocking the binding of the chemokines lymphotactin, RANTES, MIP-1-alpha, MCP-1, MCP-4, IL-8, HIP-10, factakline, and SLC.

Applicants submit that one of skill in the art can readily identify chemokines. Moreover, Applicants have provided evidence the M3 protein of MHV68 can be used to block the binding of not one, not two, not three, but nine members of the genus (chemokines). This fact is acknowledged in the Office action. Furthermore, the specification provides guidance as to the identity of these other chemokines (for example, murine KC, murine MIP2, human GCP2, see the specification at page 2, lines 19-23), a fact which is also acknowledged in the Office action.

The number and variety of examples is irrelevant if the disclosure is "enabling" and sets forth the "best mode contemplated." (*In re Borkowski et al.* (CCPA 1970) 442 F.2d 904, 164 USPQ 642). In addition, a disclosure which contains representative examples which provide reasonable assurance to one of skill in the art that the agents falling within the scope of claim will have the alleged utility is all that is required, when there is no reason to suspect that the assertions are not accurate (*In re Barr et al.* (CCPA 1971) 444 F.2d 558, 1709 USPQ 330). Given that nine examples are disclosed in the specification, Applicants submit that one of skill in the art would be reasonably assured that the specification is enabling for agents falling in the scope of the claims.

The predecessor of the Federal Circuit has held that nothing is gained by repetitive examples which each assert the same kind of biological activity for every compound embraced by a broad claim (*In re Surrey* (CCPA 1966) 370 F.2d 349, 151 USPQ 724), and that an applicant need not provide a specific example of everything embraced by broad claims (*In re Anderson* (CCPA 1973) 471 F.2d 1237, 176 SUPA 331). In fact, a single illustrative embodiment may suffice when the invention claimed is for a known class of compounds (*In re Herschler* (CCPA 1979) 591 F.2d 693, 200 USPQ 711). Generally, the Patent office requires that at least one working example be provided as part of the disclosure of the specification (37 C.F.R § 1.71(b)). Thus Applicants submit that evidence provided by nine examples is more than sufficient to provide support for the claims.

The specification (see Fig. 1 and page 9, lines 12-15) discloses that the M3 protein binds MIP-1 (CC chemokine) Fractalkine (CXC3 chemokine) and Il-8 (CXC chemokine). Fig. 2 shows that the binding of M3 to RANTES can be competed by a number of chemokines inhibitors tested, which include CXC, CC, C, and CX3C inhibitors, and human and mouse chemokines. Lane 2 is the binding in the absence of the competitor, and a very strong band can be seen. In lane 3, human RANTES is used as the competitor, and no bands can be seen. An additional copy of Fig. 2 is provided for the Examiner's convenience.

The Office action alleges that the data shown questions the binding of the chemokines murine KC, murine MIP-2, and murine LIX. Applicants respectfully disagree with this assertion. The assay shown is a *competition assay*, using labeled human RANTES. A competition assay is based on binding affinities. The results demonstrate that unlabeled human RANTES fully competes for M3 binding of labeled human RANTES. In addition, human MIP-1 and murine MIP-1 compete for M3 binding. A smaller band is seen when murine KC, murine MIP-2, and murine LIX are used in the competition assay. A band of a smaller size or lower intensity may demonstrate that a chemokine binds M3, and competes with labeled RANTES for binding to M3. Applicants do not deny the appearance of a band when murine KC, murine MIP-2, and murine LIX are used indicates that the affinity of these chemokines for M3 may be less than the affinity of human RANTES for M3 (by comparison with lane 3, where no band can be seen), or that these chemokines may bind to a different region of M3 than RANTES. However, although the assay demonstrates that there may be differences in binding affinities, or binding sites, the assay most certainly does not negate the Applicants discovery that M3 can be used to block the binding of a chemokine to a receptor.

Fig. 3 of Parry et al. shows that human IL-8, human GROα, Human IP-10, human GCP-2, human MIP-1α, human RANTES, human MIP-1, human MCP-4, murine SLC compete for binding of labeled MIP-1α or labeled IL-8. Once again, the assay shown is a competition assay, which indicates that murine MIP-2 or murine LIX are unable to compete with RANTES for binding to M3. As discussed above, the apparent inability of murine MIP-2, or murine LIX to compete for binding of labeled MIP-1α or IL-8 only indicates a different binding affinity or a different binding, than RANTES.

Furthermore, without conceding that the Examiner's assertion is correct, Applicants also note that the potential of inoperative embodiments is not sufficient to bar a generic claim (*In re Angstadt*, 537 F.2d 498 (1976)). Moreover, claim 15 has been amended to recite that the method is directed to

a method of blocking the binding of a chemokine to its receptor, wherein the chemokine is *capable of binding to M3*.

In view of the above arguments, reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

Applicants submit that the claims are now in condition for allowance. If any minor matters remain to be discussed, the Examiner is invited to call the undersigned at the telephone number listed below.

Respectfully submitted,

KLARQUIST SPARKMAN, LLP

By _____
Susan Alpert Siegel, Ph.D.
Registration No. 43,121

One World Trade Center, Suite 1600
121 S.W. Salmon Street
Portland, Oregon 97204
Telephone: (503) 226-7391
Facsimile: (503) 228-9446

Marked-up Version of Amended Specification and Claims
Pursuant to 37 C.F.R. §§ 1.121(b)-(c)

In the specification:

On page 1, line 1, please delete the title:

[VIRAL PROTEIN BINDING COMPOSITIONS AND METHODS]

And insert therefor:

USE OF THE M3 PROTEIN OF MHV68 TO BLOCK BINDING OF A CHEMOKINE TO ITS RECEPTOR

Please delete the following paragraphs found on pages 7-8 of the specification:

[Figure 1 shows auto-radiographs of SDS-PAGE analysis, with molecular masses in kDa, from experiments in which soluble chemokine binding activity is produced by MHV68.

Figure 2 shows a further auto-radiograph of another SDS-PAGE analysis from an experiment to show binding specificity of the soluble chemokine binding protein encoded by the MHV68 M3 ORF.

Figure 3 is a graph showing binding of [125I] RANTES to test (U937) cells in the presence of different amounts of MHV68-infected cell supernatants expressed as cell equivalents.

Figure 4 comprises two graphs (4 (a) and 4 (b)) showing binding of MIP-1 alpha and IL-8 to U937 cells.

Figure 5 is an auto-radiograph of SDS-PAGE analysis experiments involving binding of M3 to MIP-1 alpha and IL-8.

Figures 6 and 7 are graphs showing results of inhibition experiments with M3, cultured cells and chemokines.

Figure 8 is a graph showing results of in-vivo experiments for the effect of M3 on inflammatory responses in mice.]

Please delete the paragraph on page 13, lines 26-21:

[The MHV68 M3 ORF was amplified from infected cell DNA by PCR using oligonucleotides 5'-CGCGAATTCATGGCCTTCCTATCCACATCG-3' inserting an EcoRI site and 5'-GGTGCGGCCGCATGATCCCCAAAATACTCCAGC-3' which inserts a NotI site. The 1238 base pair product was digested with EcoRI and NotI and before being ligated in to EcoRI, NotI digested pBAC-1 (Novagen) creating pBACM3. The ORF was]

And insert therefor:

The MHV68 M3 ORF was amplified from infected cell DNA by PCR using oligonucleotides 5'-CGCGAATTCATGGCCTTCCTATCCACATCG-3' (SEQ ID NO: 1) inserting an EcoRI site and 5'-GGTGCGGCCGCATGATCCCCAAAATACTCCAGC-3' (SEQ ID NO:2) which inserts a NotI site. The 1238 base pair product was digested with EcoRI and NotI and before being ligated in to EcoRI, NotI digested pBAC-1 (Novagen) creating pBACM3. The ORF was

In the claims:

17. (Twice Amended) A method of blocking binding of a chemokine capable of binding an M3 protein of MHV68 to a receptor for the chemokine on the surface of a cell, comprising

contacting the cell with a M3 protein of MHV68 or functional homologue thereof which binds to the chemokine, thereby blocking the binding of the chemokine to the receptor.

18. (Reiterated) The method of claim 17, wherein the chemokine is a CXC, CC, C, or a CX3C chemokine.

19. (Reiterated) The method of claim 18, wherein the chemokine is a human or a mouse chemokine.

20. (Twice Amended) The method of claim 17, wherein the chemokine is lymphotactin, RANTES, MIP-1 alpha, MCP-1, MCP-4, IL-8, murine KC, murine MIP2, human GCP2, human IP10, [fractaline] fractalkine, murine LIX, MIP-1, or secondary lymphoid tissue chemokine SLC.

22. (Reiterated) The method of claim 17, wherein the cell is *in vitro*.

23. (Reiterated) The method of claim 17, wherein the cell is *in vivo*.

24. (Amended) The method of claim 17, wherein the M3 protein of MHV68 is labeled.

25. (Reiterated) The method of claim 17, wherein the chemokine is labeled.

26. (Reiterated) The method of claim 17, wherein the receptor for the chemokine is labeled.

27. (Reiterated) The method of claim 17, wherein the cell is a skin cell.

28. (Amended) The method of claim 17, wherein the M3 protein of MHV68, or homologue is a coupled protein.

Please add the following new claims:

29. (New) The method of claim 17, wherein the chemokine comprises lymphotactin.

30. (New) The method of claim 17, wherein the chemokine comprises RANTES.

31. (New) The method of claim 17, wherein the chemokine comprises MIP-1-alpha.

32. (New) The method of claim 17, wherein the chemokine comprises MCP-1.

33. (New) The method of claim 17, wherein the chemokine comprises MCP-4.

34. (New) The method of claim 17, wherein the chemokine comprises IL-8.

35. (New) The method of claim 17, wherein the chemokine comprises human GCP2.

36. (New) The method of claim 17, wherein the chemokine comprises human IP10.

37. (New) The method of claim 17, wherein the chemokine comprises fractalkine.

38. (New) The method of claim 17, wherein the chemokine comprises secondary lymphoid tissue chemokine SLC.